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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/812,238	03/29/2004	Kishore K. Wary	D6563	3362

7590 10/13/2006

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EXAMINER

HADDAD, MAHER M

ART UNIT	PAPER NUMBER
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1644

DATE MAILED: 10/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Advisory Action</b> <b>Before the Filing of an Appeal Brief</b>	<b>Application No.</b> 10/812,238	<b>Applicant(s)</b> WARY ET AL.	
	<b>Examiner</b> Maher M. Haddad	<b>Art Unit</b> 1644	

**--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

THE REPLY FILED 15 September 2006 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☒ The period for reply expires 4 months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
- Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**NOTICE OF APPEAL**

2. ☐ The Notice of Appeal was filed on \_\_\_\_\_. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

**AMENDMENTS**

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
- (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
- (b) ☐ They raise the issue of new matter (see NOTE below);
- (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
- (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.
6. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
- The status of the claim(s) is (or will be) as follows:
- Claim(s) allowed: None.
- Claim(s) objected to: None.
- Claim(s) rejected: 8,9,14,15,20,21 and 32.
- Claim(s) withdrawn from consideration: None.

**AFFIDAVIT OR OTHER EVIDENCE**

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

**REQUEST FOR RECONSIDERATION/OTHER**

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because:  
See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). \_\_\_\_\_
13. ☐ Other: \_\_\_\_\_.

Continuation of 11. does NOT place the application in condition for allowance because: 1. Claim 15 stands rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inhibiting cell-cell interaction or a method of treating inflammation or angiogenesis comprising contacting the cells with an antibody directed against the sequence consisting of SEQ ID NO: 41 or the SEQ of SEQ ID NO: 2, wherein said peptide is derived from human VCIP of SEQ ID NO: 14, wherein said antibody blocks binding of  $\alpha v\beta 3$  and  $\alpha 5\beta 1$  integrins to VCIP, thereby inhibiting the cell-cell interaction; does not reasonably provide enablement for a method of treating a patient with any pathological condition caused by integrin-mediated cell-cell interaction, comprising administering to said patient an antibody directed against a peptide consisting of SEQ ID NO: 41 or SEQ ID NO: 2 that is derived from a cell surface VCIP consisting of SEQ ID NO: 13, wherein said antibody blocks binding of  $\alpha v\beta 3$  and/or  $\alpha 5\beta 1$  integrins to the cell surface VCIP, thereby treating the patient with the pathological condition caused by the integrin-mediated cell-cell interaction in claim 15. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with this claim for the same reasons set forth in the previous Office Action mailed 5/31/06.

Applicant's arguments, filed 9/15/06, have been fully considered, but have not been found convincing.

Applicant disagrees with the Examiner that the specification is not enabled for treating any pathological condition because the pathological conditions recited in the instant claims are inflammation or tumor. However, Applicant argues limitations not recited in instant claim 15. Claim 15 reads on any pathological conditions caused by integrin-mediated cell-cell interaction.

2. Claims 8-9 and 14 stand rejected under 35 U.S.C. 102(b) as being anticipated by Vassilev et al (Blood. 1999 Jun 1;93(11):3624-31), as is evidenced by Bendayan (J. Histochem. Cytochem. 1995, 43:881-886) for the same reasons set forth in the previous Office Action mailed 5/31/06.

Applicant's arguments, filed 9/15/06, have been fully considered, but have not been found convincing.

Applicant argues that Vassilev et al neither taught that the antibody was directed against the 5 amino acid peptide of SEQ ID NO: 41 or the amino acid peptide of SEQ ID NO: 2 nor did it teach that the peptide was derived from VCIP as disclosed by the instant specification. However the anti-RGD antibody taught by Vassilev et al would bind the claimed SEQ ID NOS: 2, 41 and SEQ ID NO: 13 because all said sequences contain RGD sequence in them.

Applicant further argues that Vassilev et al teach that the antibody was directed against a 10-amino acid peptide containing the RGD motif. Applicant argues that although the peptide of Vassilev et al and those of the instant invention comprise RGD sequence, the rest of the amino acids within these peptides are different. Applicant concludes that the peptides differ not only in the number of amino acid residues but also in the type of amino acids. Applicant further submits that Vassilev et al do not teach that the antibody was also directed against the claimed 5-amino acid peptide of SEQ ID NO: 41 or the 20 amino acid peptide of SEQ ID NO: 2.

Contrary to Applicant assertion, the referenced anti-RGD antibodies were not raised against a peptide of 10 amino acid in length, but rather was purified by said peptide. However, Vassilev et al, on page 3625, 1st col., under Binding assays, teaches that binding of anti-RGD antibodies to the peptide and to proteins expressing the RGD sequence was assessed by ELISA. Further Vassilev et al on page 3626, 1st col., 1st para, that the affinity purified anti-RGD fraction of IVIG bound to Fn, Fg, Vitronectin, VWF and laminin in a dose-dependent manner teaches that the RGD containing. Accordingly the referenced antibodies would bind claim SEQ ID NO: 2, 41 and 13 in absence to evidence to the contrary.

Further Applicant argues that a peptide with 10 amino acids will fold differently compared to the peptide with 5 or 20 amino acids, thereby affecting the orientation of the amino acids within the epitope that is recognized a particular antibody. Applicant submits that the antibody directed against a peptide with 10 amino acids may or may not cross-react with a peptide with 20 or 5 amino acids in length.

However, given that the referenced antibodies were able to bound to Fn, Fg, vitronectin, vWF and laminin in a dose-dependent manner, the skilled in the art would expect the the referenced antibody to bind to the claimed SEQ ID NOS: 2, 41 and 13. Further, the Examiner notes that the short peptides of 5, 10 or 20 amino acids in length do not fold.

3. Claims 15, 20-21 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Pat. No. 5,807,819 in view of U.S. Pat. No. 5,567,440 and Vassilev et al as is evidenced by Bendayan (J. Histochem. Cytochem. 1995, 43:881-886) for the same reasons set forth in the previous Office Action mailed 5/31/06.

Applicant's arguments, filed 9/15/06, have been fully considered, but have not been found convincing.

Regarding the motivation Applicant argues that the combined teachings of the references would motivate one of skill in the art to use a 10 amino acid peptide to generate an antibody that recognized the RGD motif rather than the 20 or 5 amino acid peptides of the instant invention.

However, the Examiner notes that there is no need for a motivation to make an antibody to either SEQ ID NO: 2 or 41 because Vassilev's antibodies would bind the claimed sequences, what is really required in order to meet a prima facie obvious is to substitute the CRGDDVC cyclic peptide taught by the '819 patent with anti-RGD antibody taught by Vassilev et al in a method of inhibiting angiogenesis in a subject to arrive to the claimed invention as set forth in the previous Office Actions.

*Maher M. Haddad*  
MAHER M. HADDAD  
PATENT EXAMINER